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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/144,838	08/31/1998	MICHAEL A. SIANI	GRFN-020/01U	5261

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EXAMINER	
CELSA, BENNETT M	

ART UNIT	PAPER NUMBER
1639	40

DATE MAILED: 02/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

File copy

Office Action Summary	Application No.	Applicant(s)	
	09/144,838	SIANI ET AL.	
	Examiner	Art Unit	
	Bennett Celsa	1639	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,29,31,32,36 and 52-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,29,31,32,36 and 52-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

Applicant's amendment dated 10/21/03 in paper no. 39 is acknowledged.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. NOTE: applicant's newly presented claims 37-66 (which were previously presented and canceled) have been renumbered as claims 52-81, respectively. See MPEP Rule 111.

Information Disclosure Statement

Applicant requested Examiner consideration of references not previously considered by the Examiner. Applicant was requested to provide a new 1449 listing references and enclose reference and listing of references which were not previously considered by the Examiner. *The 1449 was not included with applicant's amendment and has not yet been received by the Examiner.*

Status of the Claims

Claims 28-29, 31, 32, 36 and 52-81 are currently pending. are currently pending and under consideration.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objection (s) and/or Rej ction (s)

Applicant's amendment, arguments and imminent submission of a terminal disclaimer has obviated the new matter rejection, written description and prior art rejections of record, however the double patenting rejection is still pending. Accordingly, the new matter and prior art rejections of record are hereby withdrawn; and the double patenting rejections will be withdrawn upon the receipt of proper terminal disclaimer(s) by the Examiner as promised by applicant.

Outstanding Objection(s) and/or Rejection (s)

Double Patenting

4. Claims 28-29, 31, 52-61 and 71-81 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims (e.g. claims 1-7) of U.S. Patent No. 6,184,344 in view of Canne et al., JACS Vol. 117 (1995) pages 2998-3007.

The Patent claims teach native chemical ligation approach (e.g. head to tail ligation) of a first and second oligopeptide, with the preferred embodiment being the derivation of such oligopeptides from chemokines (e.g. IL-8: see fig. 7; and examples).

The patent claims fail to teach the use of oligopeptide fragments from different chemokine proteins (e.g. comprising a functional protein module) to form a cross-over (e.g hybrid) proteins .

However, the Canne et al. Reference disclose a chemical ligation chemoselective method of making both **hetero-** and homo- **dimers** utilizing a "***modular strategy***" (abstract) (emphasis provided). The Canne et al. method extends the native peptide ligation (e.g. see page 2999, beginning of left paragraph and citation no. 13 to

Science article: herein the "Science article") (which is synonymous with the patented claim method) chemoselective technique to other ligation chemistries (e.g. thioesters, oximes, hydrazones, disulfides, thiazolidones etc.: see page 2999 left column) and to the formation of "complex protein analogues" (not just single protein syntheses as described in the Science article) which would allow for the condensation or more than two (e.g. "Three or more") unprotected **peptide segments** in a specific manner utilizing chemical ligation (emphasis provided). Accordingly, the Canne et al. Reference suggests the use of chemoselective chemical ligation to condense two or more peptide segments once or in a multiple manner using the native chemical ligation strategy (e.g. in the Science article) and/or different chemoselective ligation chemistries.

Accordingly, the Canne reference teaching of the use of chemoselective chemical ligation (e.g. including native chemical ligation) in a modular strategy to generate heterodimers utilizing two or more fragments of transcriptional regulatory proteins (e.g. cMyc and Max) that comprise protein domains (e.g. see schemes and figures especially schemes 1 and 3) would motivate one of ordinary skill in the art to utilize the patented claim process in the Canne modular strategy and thus render obvious the presently claimed invention..

5. Claims 32, 36 and 62-70 are rejected under 35 U.S.C. 103(a) as being rejected for obviousness-type double patenting over U.S. Patent No. 6,184,344 in view of Canne et al., JACS Vol. 117 (1995) pages 2998-3007 as applied to claims 28-29, 31, 52-61 and 71-81 above, and further in view of Pavia et al., Biorg. & Medicinal Chem. Lett. Vol. 3, No. 3 pages 387-396.

The '344 and Canne et al. combined teaching of making prospective analogues (e.g. ligands) by chemical ligation of peptide fragments one at a time for biological evaluation differs from the presently claimed invention (e.g. claims 32-36) which is drawn to the making and screening of libraries of ligands for biological evaluation.

However, the Pavia et al. reference teaches that the traditional serial process of synthesizing and testing peptide analogues one at a time is being replaced by the use of combinatorial library syntheses strategies since the libraries provide the ability to increase molecular diversity and utilize high throughput screening which optimizes drug discovery See e.g. Pavia et al. Abstract; page 391 ("Automated Methods").

Accordingly, one of ordinary skill in the art would be motivated to generate libraries of compounds by utilization of the '344 and Canne et al. reference method in order to optimize drug discovery.

Thus, modification of the '344 and Canne et al. reference method technique to utilize combinatorial libraries would have been obvious to one of ordinary skill in the art at the time of applicant's invention in order to optimize drug discovery.

6. Claims 28-29, 31, 52-61 and 71-81 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims (e.g. claims 1-7) of U.S. Patent No. 6,326,468 in view of Canne et al., JACS Vol. 117 (1995) pages 2998-3007.

The Patent claims teach native chemical ligation approach (e.g. head to tail ligation) of a first and second oligopeptide.

The patent claims fail to teach the use of oligopeptide fragments from different proteins (e.g. comprising a functional protein module) to form a cross-over (e.g hybrid) protein .

However, the Canne et al. Reference disclose a chemical ligation chemoselective method of making both **hetero-** and homo- **dimers** utilizing a "***modular strategy***" (abstract) (emphasis provided). The Canne et al. method extends the native peptide ligation (e.g. see page 2999, beginning of left paragraph and citation no. 13 to Science article: herein the "Science article") (which is synonymous with the patented claim method) chemoselective technique to other ligation chemistries (e.g. thioesters, oximes, hydrazones; disulfides, thiazolidones etc.: see page 2999 left column) and to the formation of "complex protein analogues" (not just single protein syntheses as described in the Science article) which would allow for the condensation or more than two (e.g. "Three or more") unprotected **peptide segments** in a specific manner utilizing chemical ligation (emphasis provided). Accordingly, the Canne et al. Reference suggests the use of chemoselective chemical ligation to condense two or more peptide segments one or in a multiple manner using the native chemical ligation strategy (e.g. in the Science article) and/or different chemoselective ligation chemistries.

Accordingly, the Canne reference teaching of the use of chemoselective chemical ligation (e.g. including native chemical ligation) in a modular strategy to generate heterodimers utilizing two or more fragments of transcriptional regulatory proteins (e.g. cMyc and Max) that comprise protein domains (e.g. see schemes and figures especially schemes 1 and 3) would motivate one of ordinary skill in the art to

utilize the patented claim process in the Canne modular strategy and thus render obvious the presently claimed invention..

7. Claims 32, 36 and 62-70 are rejected under 35 U.S.C. 103(a) as being rejected for obviousness-type double patenting over U.S. Patent No 6,326,468 in view of Canne et al., JACS Vol. 117 (1995) pages 2998-3007 as applied to claims 28-29, 31, 52-61 and 71-81 above, and further in view of Pavia et al., Biorg. & Medicinal Chem. Lett. Vol. 3, No. 3 pages 387-396.

The '468 and Canne et al. combined teaching of making prospective analogues (e.g. ligands) by chemical ligation of peptide fragments one at a time for biological evaluation differs from the presently claimed invention (e.g. claims 32-36) which is drawn to the making and screening of libraries of ligands for biological evaluation.

However, the Pavia et al. reference teaches that the traditional serial process of synthesizing and testing peptide analogues one at a time is being replaced by the use of combinatorial library syntheses strategies since the libraries provide the ability to increase molecular diversity and utilize high throughput screening which optimizes drug discovery See e.g. Pavia et al. Abstract; page 391 ("Automated Methods").

Accordingly, one of ordinary skill in the art would be motivated to generate libraries of compounds by utilization of the '468 and Canne et al. reference method in order to optimize drug discovery.

Thus, modification of the '468 and Canne et al. reference method technique to utilize combinatorial libraries would have been obvious to one of ordinary skill in the art at the time of applicant's invention in order to optimize drug discovery.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 703-305-7556. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 703-306-3217. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bennett Celsa
Primary Examiner
Art Unit 1639

BC